GREGORY J. GLOVER, M.D., J.D.
FOR THE
PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA

BEFORE THE

COMMERCE, SCIENCE AND TRANSPORTATION COMMITTEE

OF THE

UNITED STATES SENATE

April 23, 2002

Mr. Chairman and Members of the Committee:

On behalf of the Pharmaceutical Research and Manufacturers of America (PhRMA), I am pleased to appear at this hearing today on the Hatch-Waxman Act. I am a physician and an attorney with the law firm of Ropes & Gray, specializing in intellectual-property and food and drug regulatory issues. PhRMA represents the country's major research-based pharmaceutical and biotechnology companies, which are leading the way in the search for new cures and treatments that will enable patients to live longer, healthier, and more productive lives.

Today, I would like to offer testimony on the importance and success of the Hatch-Waxman Act for promotion of both pharmaceutical innovation and competition, and on why S.812 as currently drafted would undermine this carefully crafted, delicately balanced regime.

PhRMA strongly believes that the U.S. pharmaceutical market is robust, competitive, and working to the benefit of consumers and patients—is working, in fact, as Congress intended when it passed the Drug Price Competition and Patent Term Restoration Act of 1984 (commonly known as the Hatch-Waxman Act after its principal sponsors). We believe that advocates of change have a heavy burden to clearly show that change is needed and would not upset the careful balance achieved by Congress. They have not met that burden.

The U.S. pharmaceutical industry continues to lead the world in pharmaceutical innovation and makes a significant contribution to the country's economy. It is a substantial contributor to the $1.3 trillion health-care sector, which, overall, accounts for about 13% of the nation's economic output, is expected to reach 16% of output by 2010, and could exceed 20%

by 2040.

Over the past 100 years, pharmaceutical research has helped transform health care, contributing substantially to an increase of nearly thirty years in life expectancy (from 47 years in 1900 to 76.5 years today). The death rate from disease has fallen by a third from 1.2 per 1,000 in 1920 to 0.8 in 1,000 per 1993, even as people live longer (sometimes succumbing to disease in later life, having benefited from control or elimination of diseases that previously struck earlier in life).

Pharmaceuticals have also brought better lives, conquering infection, making mental illness highly treatable, enhancing independence in old age, and making impressive inroads against cancer, heart disease, stroke and many other diseases. Pioneer pharmaceutical companies continue to play a critical role in addressing old and new challenges, including AIDS and Alzheimer's disease.

Not only are pharmaceuticals worth the cost, they are also cost-effective, adding little to the cost of health care and replacing less effective, more expensive treatments. Over nearly thirty years, total GDP spent on drugs rose little from only 0.84% in 1965 to 0.86% in 1992. As stated in the President's 2002 Economic Report, there is "a growing body of evidence that, for a wide range of diseases, the additional money spent on treatment is more than offset by savings in direct and indirect costs of the illnesses themselves. Indirect costs include lost productivity and, especially, poor health, which people are clearly willing to pay to avoid."

In a survey concluded this month, funded by PhRMA, of 400 physicians from throughout the country, over 90% considered the continuing development of new prescription drugs vital to patient care. In addition, 84% believed that prescription drugs have reduced the need for surgery, and 95% of these physicians thought that prescription drugs have shortened hospital stays. In addition, eight out of ten of those surveyed acknowledged brand name pharmaceutical companies as deserving the most credit for developing new prescription drugs and breakthrough cures.

The research-based pharmaceutical sector in the United States is, in fact, the single largest global player in the research and development of new drugs, both in terms of new drugs brought to market, and R&D expenditures. The research-based pharmaceutical industry in the United States is responsible for the discovery and development of over 90 percent of new drugs worldwide.

PhRMA companies spend an estimated 17.7% of sales on R & D, the highest percentage of any major U.S. industry. The pharmaceutical industry is more research intensive than the electronics, communications and aerospace industries. The typical PhRMA company spends more on research each year than such companies as Microsoft, Boeing, and IBM, as evidenced by a comparison of average research outlays reported publicly by PhRMA member companies and by Microsoft, Boeing, and IBM as stated in their annual reports. National Science Foundation studies have shown that while the pharmaceutical industry recorded only

2.5% of the domestic sales of companies that conducted R&D in 1998, it accounted for 8.7% of all company-funded R&D, 18.7% of all company-funded basic research, and 4.8% of all research scientists and engineers.

Research-based pharmaceutical companies allocate nearly 78.5% of their R&D expenditures to the research and evaluation of new drug products. The remaining 21.5% is devoted to research into significant improvements and/or modifications to existing products. Such significant adjustments can include enhanced efficacy, improved dosage and delivery forms and patient-tailored therapies.

The Hatch-Waxman Act has played a critical role. On the one hand, the generic industry has flourished since the passage of the 1984 compromise law eliminated major barriers to market entry and made it much easier, far less costly, and quicker for low-cost generic drug manufacturers to get their copies of innovator medicines to market following patent expiration.

Since 1984, the generic industry's share of the prescription-drug market has jumped from less than 20% to almost 50%.

Before 1984, it took three to five years for a generic copy to enter the market after the expiration of an innovator's patent. Today, generic copies often come to market as soon as the patent on an innovator product expires, And sales of pioneer medicines typically drop by 40% or more within weeks after generic copies enter the market.

Prior to 1984, only 35% of top-selling innovator medicines had generic competition after their patents expired. Today, almost all innovator medicines face such competition.

On the other hand, the Hatch-Waxman Act provided the research-based pharmaceutical industry—the source of virtually all new drugs in the U.S.—limited incentives to innovate, through restoration of part of the patent life lost by pioneer medicines as a result of regulatory review by the Food and Drug Administration (FDA) and litigation procedures to decrease the likelihood of patent infringing market entry of generic drug products. The research-based industry, spurred by accelerating scientific and technological advances, continues to increase its investment in R&D and to develop new, more advanced, and more effective medicines.

The research-based industry's investment in pharmaceutical R&D has jumped from $3.6 billion in 1984 to more than $30 billion this year.

During the 1990s, the research-based industry developed 370 new life-saving, cost-effective medicines - up from 239 in the previous decade.

The research-based pharmaceutical industry now has more than 1,000 new medicines in development, either in human clinical trials or at FDA awaiting approval. These include more than 400 for cancer; more than 200 to meet the special needs of

children; more than 100 each for heart disease and stroke, AIDS, and mental Illness; 26 for Alzheimer's disease; 25 for diabetes; 19 for arthritis; 16 for Parkinson's disease, and 14 for osteoporosis.

These data on generic market entry and pharmaceutical innovation demonstrate that the Hatch-Waxman compromise is both promoting competition and encouraging innovation. As a result, consumers are receiving the benefits of early access to low-cost generic copies and of an expanding stream of ever more effective and precise, sophisticated medicines.

How has the Hatch Waxman compromise both promoted competition and preserved incentives for innovation? A little history helps to explain.

Following amendments made to the Federal Food, Drug, and Cosmetic Act ("FCDA") in 1962, all new drugs had to satisfy strict pre-market approval requirements for both safety and efficacy, and, as a consequence, submit to lengthy FDA approval processes. The substantial safety and efficacy data needed to support the approval of a drug were considered to be trade-secret information that could not be used to approve competing, generic copies. Apart from repeating the long, costly clinical studies performed by an innovator company, a generic applicant could obtain approval only by using a literature-based (so-called "paper") New Drug Application (NDA), which was possible only when published scientific literature demonstrated a drug's safety and effectiveness. As a consequence, prior to 1984, there were few generic copies of pioneer drugs.

To permit the approval of generic copies of all post-1962 drugs, the Hatch-Waxman Act compromise in effect revoked the trade-secret status of innovators' safety and effectiveness information. Instead of proving safety and effectiveness, a generic manufacturer was allowed to show only that its copy is bioequivalent to a pioneer product and that FDA could, therefore, rely on the pioneer's safety and efficacy data to approve the copy. Bioequivalence means that a copy's active ingredient is absorbed at the same rate and to the same extent as that of the pioneer medicine.

As a result of the Hatch-Waxman Act, generic manufacturers are able to avoid the huge cost (estimated at over $800 million on average) of discovering and developing a new drug. It costs only a very small fraction of that amount for generic manufacturers to demonstrate bioequivalence - which is why they can market their copies at reduced prices. The Act retains only a very limited vestige of the pioneer companies' former, complete proprietary rights in these extremely valuable data. Under the Act, FDA is prohibited from approving generic copies of a pioneer drug for five years after approval of an innovator product using a new chemical entities and for three years after approval of other pioneer drugs and innovations in existing drugs.

The Hatch-Waxman Act compromise also helped generic manufacturers by overruling the patent infringement standard articulated in a 1984 Court of Appeals decision in *Roche Products, Inc. v. Bolar Pharmaceutical Co.*, the *Bolar* case. In line with prior judicial patent

law decisions, the Court had held that it constituted patent infringement for a generic company to manufacture and test a medicine before its patent expired, including for the purpose of preparing a marketing application to submit to FDA. In a unique exception to patent law, the Hatch-Waxman Act compromise allows generic manufacturers to use innovator medicines still under patent to obtain bioequivalency data for their FDA applications so they can be ready to market their copies as soon as the pioneer patents expire.

The Hatch-Waxman Act also sought to increase the number of generic copies by providing an incentive for generic manufacturers to challenge pioneer patents. The first generic manufacturer to certify to FDA that a patent on an innovator medicine is invalid or is not infringed by its product obtains 180 days of exclusive marketing rights if the copy is approved before the patent expires. During that 180-day period, the FDA cannot approve any other copies.

To attempt to balance the generic provisions, the Hatch-Waxman Act compromise provided limited incentives to pioneer companies to help spur innovation. The law restores part of the patent life - but not all - lost by innovator products as a result of FDA review:

A pioneer drug receives a half-day in restored patent life for every day the product is in clinical trials prior to review by FDA.

A pioneer drug receives day-for-day restoration of patent life for the time it is under FDA review.

However, the effective patent life of a drug cannot exceed 14 years, regardless of how much time is lost in clinical testing and review. And the total time restored is limited to no more than five years (even if more than five years is lost during drug development and review).

As a consequence, innovator drugs introduced in the 1990s, even with patent restoration, enjoyed an average effective patent life of less than 11.5 years—substantially less than the 18.5 years enjoyed by inventors of other products. (The full patent term in the U.S., as with all member nations of the World Trade Organization, is now 20 years from the date a patent application is filed with the Patent and Trademark Office).

In addition to partial patent restoration, the law also creates procedures to facilitate the efficient resolution of patent disputes before FDA approves an allegedly infringing generic copy.

One of the fundamental principles of the Hatch-Waxman Act is that a generic drug should not be able to enter the market if it infringes a valid patent. Under U.S. law, patents are presumed to be valid, and this presumption can be overcome only by clear and convincing evidence to the contrary. Moreover, under the Hatch-Waxman Act, the generic applicant is proposing to market a drug that is the same as the pioneer's. Indeed, that "sameness" is the basis for the generic applicant to use the pioneer's data to demonstrate safety and effectiveness.

If there is a patent infringement suit, it is based on an effort to market a generic copy of a pioneer product that is covered by a presumptively valid patent.

Failure to resolve patent issues prior to generic product approval presents problems for pioneer and generic manufacturers alike. The marketing of a product that is later determined to be infringing will severely and irreparably injure the pioneer's market at a magnitude that generally cannot be compensated by the infringing generic manufacturer. At the same time, the generic manufacturer is faced with the risk of having to pay crippling actual and enhanced damages for intentional infringement if it decides to market the approved product before the resolution of the patent infringement claim. In short, (in addition to being in the interest of physicians and patients who might otherwise have to address the difficulties associated with switching from the pioneer to the generic product and back again) it is in the interest of both the pioneer and the generic company to resolve all patent issues before the generic product goes to market.

Congress recognized that it would be preferable to resolve patent infringement disputes prior to FDA product approval. Accordingly, the Act establishes patent litigation provisions to benefit both pioneer and generic manufacturers. These provisions provide for: (1) patent listing to notify generics of patents that claim the pioneer's product; (2) patent certification to inform pioneers of proposed generic products that may infringe their patents; (3) up to a 30-month stay of product approval to allow for resolution of patent infringement claims; and (4) the grant of a 180-day period of market exclusivity to the first generic that successfully challenges a listed patent.

An applicant who submits a New Drug Application ("NDA") must submit information on each patent that "claims the drug or a method of using the drug . . . and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale" of the drug.

FDA publishes the submitted patent information in its official publication, *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"). The purpose of the Orange Book listings is to provide clear notice to potential generic developers of the patents (other than process patents) that cover the product and may reasonably be asserted by the innovator against the generic drug manufacturer. In doing so, it serves to protect the interests of both pioneer and generic manufacturers.

Correspondingly, the need for patent certifications arises from the legislative intent: (1) to permit the marketing of generic copies of pioneer products immediately upon the expiration of any relevant patents; (2) to encourage generic challenges of innovator patents; (3) to provide a timely, effective mechanism for patent holders to protect rights in patents alleged to be invalid or not infringed by the generic product; and (4) to prohibit FDA's approval of any abbreviated application whose marketing would infringe a valid patent covering the pioneer product, until the parties have had a meaningful opportunity to attempt to resolve the issue.

The certification requirements determine the date on which approval of an ANDA can be made effective and, therefore, the date on which commercial marketing may begin. If the applicant makes either the first certification option (no patent information has been filed) or the second (the patent has expired), approval can be made effective immediately. Under the third certification option, (generic applicant does not intend to market the generic drug until the patent expires) approval of the application can be made effective on the date the patent expires. If, however, the applicant challenges the innovator's patent and makes the fourth certification (a "Paragraph IV" certification), the applicant is required to give notice to the holder of the patent alleged to be invalid or not infringed.

Approval of an ANDA containing the fourth certification may become effective immediately only if the patent owner has not initiated a patent infringement suit within 45 days of receiving notice of the certification. If the patent holder initiates a patent infringement action in response to a Paragraph IV Certification within 45 days of receiving notice of the certification, FDA cannot approve the ANDA for 30 months, unless either the action is resolved in favor of the generic applicant or the patent expires before that time.

The first follow-on (generic) product approved through an ANDA containing a Paragraph IV Certification receives 180 days of market exclusivity during which no subsequent ANDA for the same product can be approved. The purpose of the 180-Day ANDA exclusivity is to reward a generic drug manufacturer for the expense and effort involved in challenging a listed patent of the pioneer company. Despite these intentions, however, the 180-day provision has been at the heart of most controversies under the Hatch-Waxman Act.

Although the Hatch-Waxman compromise stimulates competition and provides only limited incentives for the innovation upon which pioneer and generic pharmaceutical companies alike depend for new products to offer to consumers, generic manufacturers are advocating major changes in the legislation. We believe that, in view of the balanced nature of the law, any proponent of change has a heavy burden to clearly demonstrate that change is necessary and would not upset the delicate compromise achieved in 1984. We do not believe this burden has been met with regard to any of the changes that have been proposed. Therefore, we strongly oppose such changes that would unfairly skew the law in favor of generic manufacturers and impede the ability of the research-based industry to realize in a timely way the promises that accelerating biomedical advances hold for patients in all parts of the world.

We believe that S. 812 as it stands, reflects the unfounded arguments in support of proposals to amend the Hatch-Waxman Act. While these proposals are, ostensibly intended to speed approval of generic drugs and enhance pharmaceutical competition, the bill is unlikely to promote either of these objectives, and, if adopted, would substantially undermine the Hatch-Waxman compromise that has proven so successful.

Specifically, as elaborated more fully below, S.812 would: (1) deny effective remedies to holders of patents infringed by generic drugs; (2) change the standards to allow FDA to approve generic drugs that could not be approved under current law because they are not, in

fact, the same as the innovator drugs for which FDA has the data necessary to assess safety and efficacy; and (3) create new requirements designed to deter outside parties from submitting scientific information to FDA that could be adverse to generic drugs. In addition, the bill would revise the current system for rewarding generic companies that challenge patents on innovator drugs in a way that would result in unnecessary litigation and keep many generic drugs off the market for a six-month period.

As an initial point, it is critical to understand that, despite arguments to the contrary, data compiled by FDA conclusively show that, in the overwhelming majority of cases, generic applications have not raised or encountered any patent issues that have delayed their approval. The facts speak far themselves:

From 1984 through January 2001, *8,259 generic applications* were filed with FDA.

Of these applications, 7,781 - *94 percent* - raised no patent issues.

Only 478 generic applications - *5.8 percent* - asserted a patent issue, either challenging a patent's validity or claiming non-infringement of a patent.

Further research shows that:

Only 58 court decisions involving *just 47 patents* have been rendered resolving generic challenges to innovator patent's—a tiny fraction of the number of generic applications.

Only 3 of the patent disputes settled between innovator and generic companies have reportedly been challenged by the FTC – an infinitesimal percentage of the applications.

As to our specific concerns regarding the proposals made in S. 812, they are as follows:

First, the bill would severely impair, if not eliminate, effective remedies for patent infringement.

As explained above, under current law, FDA is barred for up to 30 months from approving a generic drug that is involved in timely initiated patent litigation. The Hatch-Waxman Act made it no longer an act of patent infringement for a generic company to use a pioneer company's patented product in preparing the marketing application for its generic copy of that product. (Such otherwise-infringing testing is not, in fact, permitted in any other U.S. industry.) Patent holders are not permitted to assert their rights against generic applicants during this period. Now, a claim for patent infringement cannot be brought until the generic company actually files its application. The 30-month stay increases the likelihood that a pioneer company will still be able to defend its patent rights before FDA approval enables an allegedly infringing generic product to come onto the market.

S. 812 would simply abolish the innovator's right to litigate patent disputes prior to FDA approval. Although an innovator could still theoretically seek a preliminary injunction from the court against the generic product, courts rarely grant preliminary injunctions in patent litigation, and such injunctions are especially difficult to obtain in the pharmaceutical patent context due to the highly complex and technical, fact-intensive claim analysis required. As a result, even though generic companies would continue to enjoy the benefits of the Hatch-Waxman Act that were created at the expense of innovator companies, the innovator industry would be denied the corresponding, necessary means provided in the Act to protect against patent infringement because of this unique privilege granted to generic companies.

The bill would also permit the approval of generic drugs that do not, in fact, duplicate their reference drugs. Present law prohibits the use of studies, other than bioequivalence data, to support an abbreviated new drug application for a generic drug. The premise of the law is that the generic drug must be the same as the innovator drug in all material respects, and therefore the only issue is showing that it is absorbed by the body at the same rate and to the same extent as the innovator drug. S. 812 would loosen the standards and allow FDA to approve generic drugs that are not the same as the reference innovator drugs, substituting FDA judgment that some unspecified differences don't matter for the current objective requirement that generic drugs must be the same as the reference innovator drugs.

In light of problems that have arisen even with application of the existing bioequivalence standard, we are quite concerned by this proposal. In this regard, we would note that two-thirds of physicians surveyed, as discussed above, considered changing bioequivalence standards to be a bad idea, primarily because of the importance of maintaining the quality of the drugs and protecting the safety of their patients.

In addition, the bill would inhibit the submission of citizen petitions offered in good faith to inform the Agency of legitimate concerns regarding a proposed drug product.

S. 812 would impose new burdens on use of the citizen petition, which is the mechanism by which an outside party can request an official FDA decision on a scientific or other issue. Under the bill, it appears that the Federal Trade Commission (FTC) may be *required* to open an investigation of any person submitting a citizen petition to FDA if anyone alleges that the citizen petition has been submitted for an improper purpose.

Such mechanisms would deter persons from submitting citizen petitions to the FDA containing scientific or other relevant information regarding a competing product, since an FTC investigation, accompanied by a subpoena for documents, would seem to be the inevitable and immediate result. Congress and FDA should welcome a process for airing scientific issues, rather than trying to inhibit discussion. If a party were to submit a baseless citizen petition to achieve an anti-competitive effect, the existing anti-trust laws would provide ample bases for the FTC, or a private party, to bring an enforcement action. S. 812 would serve only to chill legitimate petitioning, to the detriment of the FDA approval process, undermining the legitimate economic interests of competitors and, potentially, putting consumers at risk.

The bill would as well revise the requirements for obtaining generic drug exclusivity in a manner that would keep more rival generic products off the market longer and promote unnecessary litigation. In an apparent inconsistency with its stated objective of speeding generic drug approvals, S. 812 would enhance the ability of the first generic drug company that challenges an innovator patent to keep all other generic products off the market for six months. A provision for six months of exclusivity exists in current law but has been made less capable of keeping other generics off the market. S. 812 would overrule those decisions.

In summary, the Hatch-Waxman Act is one of the most successful pieces of consumer legislation in history. The law works. Contrary to the assertions of others, S. 812 would not close loopholes, it would undermine the Act's few, critical protections for innovator intellectual property rights. Without these protections, there will be less innovation, fewer new drugs for generics to copy and, more importantly, fewer new drugs to enhance treatment for patients.

This concludes my written testimony. I would be pleased to answer any questions or to supply any additional materials requested by Members or Committee staff on these or any other Issues.